

## **REMARKS**

Applicants have the following response to the Office Action in the order in which the items appear in the Office Action. Applicants have minor amendments to the claims to remove informalities therein. It is not believed that such amendments are Festo-type narrowing amendments.

### **I. Oath/Declaration**

The Examiner states that the oath or declaration for the present application is defective. Accordingly, Applicants are submitting a new Declaration which incorporates therein the language requested by the Examiner. Hence, it is requested that this objection now be withdrawn.

### **II. Priority**

The Examiner also states that Applicants have not complied with the conditions for receiving benefit of an earlier filing date. Applicants have now amended the specification in accordance with the Examiner's suggestion. Therefore, it is requested that this objection now be withdrawn.

### **III. Claim Objections**

The Examiner also objects to Claims 12 and 20 under 37 CFR 1.75(c), as being of improper dependent form for allegedly failing to further limit the subject matter of a previous claim. In particular, the Examiner states that the claims recite that "said green light has a wavelength of between 500 nm and 600 nm" which the Examiner alleges does not further limit Claim 11 or Claim 19 (for which these claims are dependent upon) because the Examiner alleges this limitation is a normally occurring characteristic of the green light of Claims 11 and 19.

In order to advance the prosecution of this application, Applicants have now amended Claim 12 to be dependent on Claim 1 and to not recite the phrase "green light". Applicants have also canceled Claim 20. Hence, it is believed that this rejection has now been overcome, and it is respectfully requested that the rejection be withdrawn.

#### **IV. Claim Rejections - 35 USC §112**

The Examiner further rejects Claims 6-10, 13-16, 26-29, 33 and 37 under 35 U.S.C. 112, second paragraph, as being indefinite. As explained in detail below, Applicants have now amended the claims and respectfully traverse the rejection.

##### **A. Claims 13-16**

The Examiner objects to Claims 13-16 and states that they provide for the use of a halogenated xanthene in the preparation of a medicament, but do not make it clear what method/process applicant is intending to encompass. Further, the Examiner states that the claim is indefinite or alternatively, improper under 35 USC §101, for setting forth a use without setting forth any steps in the process.

Applicants have amended independent Claim 13 to add the step of "adding said halogenated xanthene to a delivery vehicle". Applicants also have clarified the use of the halogenated xanthene in Claim 13 as a photoactive component in the cited medicament. Applicants believe this redresses the Examiner's basis for rejection these claims under §§ 101 and 112.

**B. Claims 6, 7-10, 14, 26-29 and 37**

The Examiner also asserts that Claims 6, 7-10, 14, 26-29 and 37 comprise improper Markush groups.

With regard to Claims 6 and 26, the Examiner states that these claims recite some items in plural form. Therefore, the Examiner invites Applicants to amend the claims to clarify this point and whether the term "proteins" encompasses multiple elements. Applicants have amended each of these claims to make each element recited therein plural and to provide the appropriate modifiers for other terms in question. It is respectfully submitted that these amended claims are not indefinite.

With regard to Claims 7-10, 14, 26-29 and 37, the Examiner objects to these claims as reciting plural elements and provides a suggestion for amending these claims. Applicants have followed the Examiner's suggestion in amending these claims. Hence, it is believed that these amended claims are not indefinite.

Finally, the Examiner objects to the terms "conditions affecting" and "related organs" in Claims 10, 33 and 37. Applicants have changed the term "conditions affecting" to -- diseases of --. With regard to the term "related organs", Applicants respectfully submit that one skilled in the art would understand this term. Further, the metes and bounds of these terms are adequately defined throughout the specification of the present application. For example, the "\_\_\_ and related organs" are explained in detail throughout the specification such as in the following passage:

**"2. Methods and medical use of the subject medicament for treatment of conditions affecting the skin and related organs.**

"The applicants have discovered that the medicaments disclosed herein are broadly applicable to improved treatment of various conditions affecting the skin and related organs of humans and animals. The medicament can be applied directly to, or substantially proximal to, tissues to be treated, including those of the skin, nails,

scalp and oral cavity. Example indications include treatment for: Psoriasis and Pustular Psoriasis; ....” (Page 12, lines 16-22)

As this passage makes clear, “skin and related organs” comprises the skin, nails, scalp and oral cavity, while “conditions affecting” such “skin and related organs” comprise diseases, such as psoriasis and pustular psoriasis, that afflict the skin and related organs. Similar support for the remainder of Claims 10, 33 and 37 can be found at page 13, line 20 - page 18, line 25. Hence, Applicants respectfully submit that amended Claims 10, 33 and 37 are not indefinite under 35 U.S.C. 112, second paragraph.

For at least the above-stated reasons, it is respectfully submitted that the §112 and §101 rejections have been overcome, and it is requested that these rejections now be withdrawn.

**V. Claim Rejections - 35 USC §102**

**A. Rejection Over Gaboury et al.**

The Examiner also rejects Claims 1, 5-6, 11-14, 16-17, 19-22, 25-26 and 30-35 under 35 U.S.C. §102(b) as being anticipated by two Gaboury et al. references (i.e., US 5,556,992 and US 5,773,460, henceforth Gaboury). This rejection is respectfully traversed.

Gaboury is directed to certain uses for certain rhodamine derivatives.<sup>1</sup> Applicants respectfully submit that Gaboury is not relevant to the claimed invention of the present application for at least several reasons, as detailed below, and thus does not anticipate nor render obvious the claimed invention.

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<sup>1</sup> Gaboury et al. (USP 5,556,992 and 5,773,460) disclose various uses for certain derivatives of rhodamine B and rhodamine 110, specifically certain esters and halogenated forms of these molecules.

The rhodamine derivatives disclosed in Gaboury are unrelated to, and readily distinguishable from, the halogenated xanthenes disclosed and claimed in the present application.

The specification and drawings for the present application clearly define the halogenated xanthenes claimed herein. For example, Fig. 1a shows the generalized chemical structure of the halogenated xanthenes while Fig. 1b shows the chemical structure of Rose Bengal, a specific halogenated xanthene claimed herein. Table 1 of the specification summarizes selected chemical and physical properties (such as the chemical constituents at positions X, Y, and Z and the functionalities R<sup>1</sup> and R<sup>2</sup>, along with molecular weight and photochemical characteristics) of representative halogenated xanthenes of the present invention.<sup>2</sup> These "halogenated xanthenes", as defined in the present application, are weakly acidic (i.e., anionic) derivatives of fluorescein, having a carboxyl group at position 2', and hydroxy groups at positions 6 and 3.<sup>3</sup> This identification of the "halogenated xanthenes", as claimed in the present application, is clearly described for example by the following passage from the specification:

"1. Properties of the preferred photoactive components and medicament formulations.

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<sup>2</sup> Table 1 lists "Fluorescein." This compound was inadvertently listed as a halogenated xanthene and inadvertently listed in Claims 4 and 24. As explained herein, the halogenated xanthenes of the present application are weakly acidic (i.e., anionic) derivatives of fluorescein. Clearly, fluorescein cannot be a derivative of itself. Therefore, Applicants have now amended Table 1 and Claims 4 and 24 to remove reference thereto.

<sup>3</sup> For background on this aromatic ring numbering convention, see e.g. D.C. Neckers, Rose Bengal, *J. Photochem. Photobiol. A*, 47 (1989) 1-29. This reference was cited in some of the parent applications. A copy of the reference is attached hereto, and the reference is being cited in an IDS, being submitted within the next few days, to submit all of the references from the parent applications which are not already of record.

Neckers describes the many fundamental chemical and physical properties of the halogenated xanthenes, particularly Rose Bengal. It does not disclose or suggest the present invention.

"The applicants have discovered that a certain class of photoactive agents are broadly applicable for producing topically-applicable medicaments for treatment of certain human and animal tissues. These photoactive agents *are referred to as halogenated xanthenes and are illustrated in Figure 1a*, where the symbols X, Y, and Z represent various elements present at the designated positions, and the symbols R<sup>1</sup> and R<sup>2</sup> represent various functionalities present at the designated positions.

"Selected chemical and physical properties (such as the chemical constituents at positions X, Y, and Z and the functionalities R<sup>1</sup> and R<sup>2</sup>, along with molecular weight and photochemical characteristics) of representative halogenated xanthenes are summarized in attached Table 1." (Page 5, line 17 - page 6, line 3, emphasis added)

The background on this structure and the nomenclature of "halogenated xanthenes" is known.

See e.g. Neckers, pp. 1-3.

As is clearly illustrated in Figs. 1a and 1b of the present application, *all* halogenated xanthenes contain at least five (5) oxygen atoms, divided between the carboxyl group at position 2', the oxygen functionalities at positions 6 and 3, and a heterocyclic oxygen located between positions 4 and 5.

In contrast, the rhodamine derivatives of Gaboury constitute cationic derivatives of rhodamine.<sup>4</sup> Thus, the rhodamines are weak bases, not weak acids (as is the case for the halogenated xanthenes). The rhodamines contain three (3) oxygen atoms: two oxygen atoms in a carboxyl group at position 2', and one heterocyclic oxygen between positions 4 and 5. In contrast to the halogenated xanthenes, the rhodamines lack oxygen functionalities at positions 6 and 3, replacing these hydroxy groups with amino and imino groups.

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<sup>4</sup>The structural diagrams in cols. 8 and 9 of Gaboury (US 5,773,460) illustrate the chemical structure of the rhodamines disclosed in Gaboury. Comparison of this structure with that of the halogenated xanthenes of the present application, as illustrated in Figs. 1a and 1b of the present application, graphically demonstrates that the rhodamines are unrelated to the halogenated xanthenes.

Since the aromatic core of the halogenated xanthenes and the rhodamines is identical, the full chemical name of both families contains the common root "-xanthen-9-yl". However, the rhodamines are more fully described by the root "-6-amino-3-imino-3H-xanthen-9-yl", while the halogenated xanthenes of the present invention are described by the root "-3,6-dihydroxy-9H-xanthen-9-yl". The terminology "-6-amino-3-imino-" used with the rhodamines is indicative that all rhodamine derivatives contain amino and imino groups at positions 6 and 3 (as opposed to the hydroxy groups at these positions in the halogenated xanthenes, which are described by the terminology "-3,6-dihydroxy-", indicative of the presence of such hydroxy groups).

Hence, the present application clearly defines the chemical structure of the "halogenated xanthenes" (i.e., "-3,6-dihydroxy-9H-xanthen-9-yl" compounds, as illustrated in Figs. 1a and 1b) claimed in the present application. This chemical structure is clearly distinguishable from that of the "rhodamine derivatives" of Gaboury (i.e., "-6-amino-3-imino-3H-xanthen-9-yl" compounds). Such distinction would be clear to one of ordinary skill in the art.

Additionally, based on the significant differences in chemistry of the two families of compounds (the halogenated xanthenes constituting weak acids, while the rhodamine derivatives constituting weak bases), the knowledge of certain chemical and biological behaviors of one family of compounds (i.e., the weakly basic rhodamine derivatives of Gaboury) cannot constitute sufficient knowledge to predict, *a priori* nor *ab initio*, the respective behaviors of a chemically different family of compounds (i.e., the weakly acidic halogenated xanthenes of the claimed invention). One of ordinary skill in the art would not expect that the properties of a family of weakly basic compounds to serve as the basis for accurately predicting the properties of an unrelated family of weakly acidic compounds.

Furthermore, a search of both cited patents of Gaboury (using the electronic version of each document archived in the USPTO public database) for the term "halogenated" or "xanthene" found no occurrences of either term in either patent. Thus, Gaboury does not, even in passing, suggest the halogenated xanthenes of the present application.

Hence, Gaboury cannot anticipate the claimed invention, which claims a medicament comprising at least one halogenated xanthene, because Gaboury describes a distinctly different family of compounds from those claimed in the present application. Further, disclosure of the chemical and biological properties of certain rhodamine derivatives by Gaboury does not render obvious the claimed invention since, given the current state of knowledge in the fields of chemistry, physics, biology, biochemistry, and medicine, it is impossible to accurately predict the relevant medicinal properties (i.e., toxicity, photochemical response, pharmacokinetics, etc.) of a particular family of compounds (specifically, the halogenated xanthenes) using knowledge of such properties for a different family of compounds (specifically, the rhodamine derivatives of Gaboury).

Therefore, it is respectfully submitted that Gaboury does not disclose or suggest the claims of the present application, and those claims are patentable thereover. Accordingly, it is requested that this rejection be withdrawn.

**B. Rejection Over Kopia**

The Examiner also rejects Claims 1, 4-12, 21, and 24-31 under 35 U.S.C. 102(e) as being anticipated by Kopia et al. This rejection is also respectfully traversed.

The Examiner cites Kopia for disclosing a composition with fluorescein isothiocyanate conjugated goat anti-rabbit antibodies and alleges that it corresponds to Applicants' claimed



medicament.<sup>5</sup> However, as explained below, Kopia does not disclose or suggest the claimed invention and is in fact, not even relevant thereto.

More specifically, Kopia uses the cited fluorescein isothiocyanate conjugate as an *in vitro* diagnostic agent to assess whether certain modified red blood cells retained antigenicity as shown in the below passage:

“To determine whether the substance P component ... was structurally unaltered and recognizable ... untreated RBCs and conjugate-labeled RBCs were analyzed to determine if ...2. Fluorescein isothiocyanate (FITC) conjugated goat anti-rabbit antibodies nonspecifically bound to the conjugate-labeled or non-labeled cells....” (col. 52, lines 21-34)

The Example in Kopia goes on to state:

“In FIG. 3B, treatment of conjugate-labeled cells with a fluoresceinated goat anti-rabbit antibody demonstrated that this antibody has only minimum non-specific binding to RBCs, as evidenced by a small increase in green fluorescent signal (LFL1) when compared to the results in FIG. 3A.” (col. 52, lns. 42-46)

No therapeutic functionality of this fluorescein conjugate is disclosed or suggested in Kopia, nor does the reference disclose or suggest any use as a topical agent for photodynamic treatment of human or animal tissue, as required in the claims of the present application. Thus, Kopia does not disclose or suggest a topical medicament for photodynamic therapy, as specifically recited in independent Claims 1 and 21 of the present invention.

Furthermore, Applicants believe that Kopia requires the use of a conjugate agent. For example, the Summary of the Invention in Kopia states:

“In accordance with one aspect of the present invention, compounds are provided having the capability of binding

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<sup>5</sup> Applicants have deleted “fluorescein” from the Markush groups of Claims 4 and 24. Since fluorescein contains no halogens, it is improper to classify it as a “halogenated xanthene.”

therapeutically active substances to lipid containing bioparticles, e.g., cells or viruses. The compounds of the invention include a bio-affecting moiety, comprising a therapeutically active substance which is stably linked via a linking moiety to at least one hydrocarbon substituent selected so as to render the compounds sufficiently non-polar that they are capable of stable binding to lipid components of lipid-containing bio-compatible particles either in vivo or in vitro. The compounds optionally include a spacer moiety to provide separation between the therapeutic substance and the linking moiety, as required to mediate therapeutic activity. “

”The compounds of the invention are further characterized by having varying but predictable stabilities of association with the lipid component of biomembranes. The compounds are sufficiently non-polar as to have a surface membrane retention coefficient (MRC) of at least 90% and a membrane binding stability of at least 30%.” (col. 5, lns. 5-24)

Further, Claim 1 of Kopia recites as follows:

“Claim 1. A compound [comprising B, R, and R<sub>1</sub> components] wherein B represents a chemotherapeutic substance; R and R<sub>1</sub> are substituents independently selected ... to impart a membrane binding stability of at least 30% to said compound....” (col. 73, lines 2-19)

Thus, Kopia requires the use of a conjugate agent.

In contrast, the independent claims of the present application do not require such a conjugate agent.<sup>6</sup> Further, the specification clearly discloses that the halogenated xanthenes can be used therapeutically without dependency upon conjugate forms, such as for example at the following passage:

“As an example ... the inventors have found that the prototypical halogenated xanthene, Rose Bengal, will accumulate preferentially in (i.e. target) some tumors and other diseased tissues and pathogens, has negligible dark cytotoxicity, high light cytotoxicity

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<sup>6</sup> Amended independent Claim 13 recites: “by adding to a delivery vehicle.” This is just dissolving it in a carrier. This is not the same as a conjugate which is a chemical derivative, where two things are chemically bonded together.

upon illumination with visible light, relatively low cost, and the ability to clear rapidly from the body.” (page 7, lines 18-22)

This passage makes it clear that the halogenated xanthenes exhibit intrinsic therapeutic function when used in non-conjugate form (i.e., Rose Bengal is not a conjugate agent) and provides support for the independent claims.

Any potential ambiguity about this feature is dispelled by the immediately succeeding section of the specification, which begins:

“Moreover, the inventors have discovered that the facility with which the halogenated xanthenes target specific tissues or other sites *can be further optimized* by attachment of specific functional derivatives at positions  $R^1$  and  $R^2$ , so as to change the chemical partitioning or biological activity of the agent. For example, attachment of one targeting moiety or more at positions  $R^1$  or  $R^2$  can be used to improve targeting to specific tissues, such as cancerous tumor tissues or sites of localized infection.” (page 8, lines 1-5, emphasis added)

Thus, the already successful use of the halogenated xanthenes as therapeutic agents can be augmented through use in conjugate form. Hence, while Kopia requires use of conjugate agents (and states such in the independent claim), the independent claims of the present application have no such requirement.

Therefore, Kopia fails to disclose or suggest the claimed invention, and thus it is respectfully requested that this rejection be withdrawn.

Accordingly, for the above-stated reasons, the claims of the present application are not anticipated by the cited references, and it is requested that the §102 rejections be withdrawn.

## **VI. Claim Rejections - 35 USC §103(a)**

Finally, the Examiner rejects Claims 2-4, 7-10, 15, 18, 23-24, 27-29, and 36-38 under 35 U.S.C. 103(a) as being unpatentable over Gaboury. In this rejection, the Examiner admits that Gaboury does not disclose the specific halogenated xanthenes of the above claims. The Examiner, however, alleges that the "halogenated xanthene compounds of Gaboury et al. are structurally similar to the compounds of the instant invention" thereby making the instant invention obvious. However, as explained *supra* in reference to the rejection under §102(b) over Gaboury, the rhodamines in Gaboury are not halogenated xanthenes and are very different and from a different chemical family than the halogenated xanthenes disclosed and claimed in the present application. It cannot be obvious to use a particular family of compounds (i.e., the halogenated xanthenes) simply because one is knowledgeable of the properties of another family of compounds (i.e., the rhodamine derivatives).

Accordingly, it is respectfully requested that the rejection of 2-4, 7-10, 15, 18, 23-24, 27-29, and 36-38 under 35 U.S.C. 103(a) as being unpatentable over Gaboury be withdrawn.

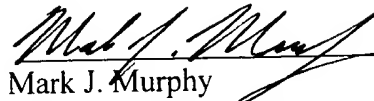
For the above-stated reasons, it is respectfully submitted that the claims of the present application are in an allowable form and are patentable over the cited references. Accordingly, it is requested that the application now be allowed.

Favorable reconsideration is earnestly solicited.

Respectfully submitted,

Date:

*July 16, 2002*



Mark J. Murphy

Registration No. 34,225

COOK, ALEX, McFARRON, MANZO,  
CUMMINGS & MEHLER, Ltd.  
200 West Adams Street, Suite 2850  
Chicago, Illinois 60606  
(312) 236-8500

Marked-up copy of the amendments made herein:

**IN THE SPECIFICATION:**

Please amend the paragraph of the specification at page 1, lns. 2-4 as follows:

This application claims the benefit of U.S. Provisional Application No. 60/149,015 filed August 13, 1999. This application [which] is a continuation-in-part of USSN 08/989,231, filed December 11, 1997[,] (now U.S. Patent No. 5,998,597 issued December 7, 1999); USSN 09/130,041, filed on August 6, 1998[,] ; USSN 09/184,388, filed on November 2, 1998[,] ; and USSN 09/216,787, filed on December 21, 1998 (now U.S. Patent No. 6,331,286 issued December 18, 2001), which are herein incorporated by reference in their entirety.

Please amend Table 1 as follows:

Table 1. Chemical, Physical and Photochemical Properties of Some Example Halogenated Xanthenes:

Compound	Substitution					MW (g)	$\lambda_{\text{max}}$ (nm)			$\alpha$ ( $\text{cm}^{-1} \cdot \text{mol}^{-1} \cdot \text{L}$ )	$\phi$ (triplet)	$\phi$ (singlet oxygen)		
	X	Y	Z	R <sup>1</sup>	R <sup>2</sup>		H <sub>2</sub> O	EtOH	MeO H			MeOH	H <sub>2</sub> O	EtOH
[Fluorescein]	[H]	[H]	[H]	[Na]	[Na]	[376]	[490]	[499]	[492]	[6.4x10 <sup>4</sup> ]	[0.03]	[0.03]	[0.03]	[0.09]
4',5'-Dichlorofluorescein	Cl	H	H	Na	Na	445	502	511				0.04	0.07	
2',7'-Dichlorofluorescein	H	Cl	H	Na	Na	445	502	511				0.04	0.07	
4,5,6,7-Tetrachlorofluorescein	H	H	Cl	H	H	470	515			2.9x10 <sup>4</sup>				
2',4',5',7'-Tetrachlorofluorescein	Cl	Cl	H	Na	Na	514	510	520				0.05	0.05	
Dibromofluorescein	Br	H	H	Na	Na	534	504	510		1.4x10 <sup>4</sup>		0.32	0.42	
Solvent Red 72	H	Br	H	H	H	490			450	1.4x10 <sup>4</sup>				
Diiodofluorescein	I	H	H	Na	Na	628	506	513		5.8x10 <sup>4</sup>		0.33	0.48	
Eosin B	NO <sub>2</sub>	Br	H	Na	Na	624	522			3.9x10 <sup>4</sup>				
Eosin Y	Br	Br	H	Na	Na	692	517	523	527	9.1x10 <sup>4</sup>	0.28	0.32	0.57	0.39
Ethyl Eosin	Br	Br	H	C <sub>2</sub> H <sub>5</sub>	K	714		532		1.1x10 <sup>4</sup>				
Erythrosin B	I	I	H	Na	Na	880	528	532	529	9.1x10 <sup>4</sup>	0.62	0.69	0.63	0.62
Phloxine B	Br	Br	Cl	Na	Na	830	541	548	547	1.0x10 <sup>5</sup>		0.40	0.63	
Rose Bengal	I	I	Cl	Na	Na	1018	547	557	556	1.0x10 <sup>5</sup>	0.76	0.86	0.75	0.76
Rose Bengal Dilithium	I	I	Cl	Li	Li	986		559						
Rose Bengal Amide	I	I	Cl	C <sub>2</sub> H <sub>5</sub>	(C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> N H	1100		563						0.74
Rose Bengal Diamide	I	I	Cl	(C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> N H	(C <sub>2</sub> H <sub>5</sub> ) <sub>3</sub> N H	1166		559						0.72
4,5,6,7-Tetrabromoerythrosin	I	I	Br	Na	Na	1195								

## IN THE CLAIMS:

Please amend the claims as follows:

Claim 1 (amended). A topically-applicable photodynamic medicament [for topical application], the medicament comprising at least one halogenated xanthene as a photoactive [primary active] component, wherein said medicament is useful for [photodynamic] treatment of diseases of human and animal tissue.

Claim 4 (amended). The medicament of Claim 1 wherein said halogenated xanthene includes at least one compound selected from the group consisting of [Fluorescein;] 4',5'-Dichlorofluorescein; 2',7'-Dichlorofluorescein; 4,5,6,7-Tetrachlorofluorescein; 2',4',5',7'-Tetrachlorofluorescein; Dibromofluorescein; Solvent Red 72; Diiodofluorescein; Eosin B; Eosin Y; Ethyl Eosin; Erythrosin B; Phloxine B; Rose Bengal; 4,5,6,7-Tetrabromoerythrosin; Mono-, Di-, or Tribromoerythrosin; Mono-, Di-, or Trichloroerythrosin; Mono-, Di-, or Tri[c]fluoroerythrosin; 2',7'-Dichloro-4,5,6,7-Tetrafluorofluorescein; 2',4,5,6,7,7'-Hexafluorofluorescein; and 4,5,6,7-Tetrafluorofluorescein.

Claim 6 (amended). The medicament of Claim 5 wherein said targeting moiety is selected from the group consisting of deoxyribonucleic acids (DNA) [DNA], ribonucleic acids (RNA) [RNA], amino acids, proteins, antibodies, ligands, haptens, carbohydrate receptors, carbohydrate [or] complexing agents, lipid receptors, lipid [or] complexing agents, protein receptors, protein [or] complexing agents, chelators, encapsulating vehicles, short-chain aliphatic hydrocarbons, [or] long-chain aliphatic hydrocarbons, [or] aromatic hydrocarbons, aldehydes, ketones, alcohols, esters, amides, amines, nitriles, azides, [and other] hydrophilic moieties and [or] hydrophobic moieties.



Claim 7 (amended). The medicament of Claim 1 wherein said medicament is formulated in a delivery vehicle selected from the group consisting of a liquid [liquids], a semisolid [semisolids], a solid [solids] and an aerosol [aerosols].

Claim 8 (twice amended). The medicament of Claim 7 wherein said vehicle is selected from the group consisting of an aqueous suspension, a non-aqueous suspension, [and] a nanoparticulate suspension, a solution, a cream, an ointment, a gel, a syrup, a suppository and a micro-droplet spray [suspensions, solutions, creams, ointments, gels, syrups, suppositories and micro-droplet sprays].

Claim 9 (amended). The medicament of Claim 1 wherein said halogenated xanthene is in a delivery vehicle that includes at least one [an adjuvant] selected from the group consisting of a builder[s], a stabilizer[s], an emulsifier[s], a dispersant[s], a preservative[s], a buffer[s], an electrolyte[s], a tissue penetrating agent[s] and a tissue softening agent[s].

Claim 10 (amended). The medicament of Claim 1 wherein said medicament is useful for the treatment of indications selected from the group consisting of diseases of [conditions affecting] the skin and related organs, diseases of [conditions affecting] the mouth and digestive tract and related organs, diseases of [conditions affecting] the urinary and reproductive tracts and related organs, diseases of [conditions affecting] the respiratory tracts and related organs, diseases of [conditions affecting] other internal and external tissue surfaces, [conditions affecting] tissue surfaces exposed during surgery, and [conditions related to] microbial or parasitic infection.

Cancel Claim 11.

Claim 12 (amended). The method of Claim 1 [11] wherein said medicament is activated using light having [green light has] a wavelength of between approximately 500 nm and 600 nm.

Claim 13 (amended). Use of a halogenated xanthene as a photoactive component in the preparation of a topical medicament for treatment of human and animal tissue using photodynamic therapy by adding said halogenated xanthene to a delivery vehicle.

Claim 14 (amended). The use of Claim 13 for preparation of a medicament for the treatment of indications selected from the group consisting of diseases of [conditions affecting] the skin and related organs, diseases of [conditions affecting] the mouth and digestive tract and related organs, diseases of [conditions affecting] the urinary and reproductive tracts and related organs, diseases of [conditions affecting] the respiratory tracts and related organs, diseases of [conditions affecting] other internal and external tissue surfaces, [conditions affecting] tissue surfaces exposed during surgery, and [conditions related to] microbial or parasitic infection.

Claim 16 (amended). The use of Claim 13 wherein said medicament is for photodynamic therapy with activating light having a wavelength of between approximately 500 nm and 600 nm [green activating light].

Claim 19 (amended). The use of Claim 17 wherein said halogenated xanthene is photoactivated with light having a wavelength of between approximately 500 nm and 600 nm [green activating light].

Cancel Claim 20.

Claim 24 (amended). The pharmaceutical composition of Claim 21 wherein said halogenated xanthene includes at least one compound selected from the group consisting of [Fluorescein;] 4',5'-Dichlorofluorescein; 2',7'-Dichlorofluorescein; 4,5,6,7-Tetrachlorofluorescein; 2',4',5',7'-Tetrachlorofluorescein; Dibromofluorescein; Solvent Red 72; Diiodofluorescein; Eosin B; Eosin Y; Ethyl Eosin; Erythrosin B; Phloxine B; Rose Bengal; 4,5,6,7-Tetrabromoerythrosin; Mono-, Di-, or Tribromoerythrosin; Mono-, Di-, or Trichloroerythrosin; Mono-, Di-, or Tri[c]fluoroerythrosin; 2',7'-Dichloro-4,5,6,7-Tetrafluorofluorescein; 2',4,5,6,7,7'-Hexafluorofluorescein; and 4,5,6,7-Tetrafluorofluorescein.

Claim 26 (amended). The pharmaceutical composition of Claim 25 wherein said targeting moiety is selected from the group consisting of deoxyribonucleic acids (DNA) [DNA], ribonucleic acids (RNA) [RNA], amino acids, proteins, antibodies, ligands, haptens, carbohydrate receptors, carbohydrate [or] complexing agents, lipid receptors, lipid [or] complexing agents, protein receptors, protein [or] complexing agents, chelators, encapsulating vehicles, short-chain aliphatic hydrocarbons, [or] long-chain aliphatic, [or] aromatic hydrocarbons, aldehydes, ketones, alcohols,

esters, amides, amines, nitriles, azides, [and other] hydrophilic moieties and [or] hydrophobic moieties.

Claim 27 (amended). The pharmaceutical composition of Claim 21 wherein said pharmaceutical composition is formulated in a delivery vehicle selected from the group consisting of a liquid [liquids], a semisolid [semisolids], a solid [solids] and an aerosol [aerosols].

Claim 28 (amended). The pharmaceutical composition of Claim 27 wherein said vehicle is selected from the group consisting of an aqueous suspension, a non-aqueous suspension, [and] a nanoparticulate suspension, a solution, a cream, an ointment, a gel, a syrup, a suppository and a micro-droplet spray [suspensions, solutions, creams, ointments, gels, syrups, suppositories and micro-droplet sprays].

Claim 29 (amended). The pharmaceutical composition of Claim 21 wherein said halogenated xanthene is in a delivery vehicle that includes at least one [an adjuvant] selected from the group consisting of a builder[s], a stabilizer[s], an emulsifier[s], a dispersant[s], a preservative[s], a buffer[s], an electrolyte[s], a tissue penetrating agent[s] and a tissue softening agent[s].

Claim 30 (amended). The pharmaceutical composition of Claim 21 wherein said photodynamic therapy uses activating light having a wavelength of between approximately 500 nm and 600 nm [green activating light].

Cancel Claim 31.

Claim 32 (amended). A method of treating diseased tissue comprising:  
topically applying a medicament including at least one halogenated xanthene to or proximate  
to diseased human or animal tissue; and  
illuminating said human or animal tissue with light to photoactivate [activate] said halogenated  
xanthene present within or proximate to said tissue.

Claim 33 (amended). The method of Claim 32 wherein said diseased human or animal tissue  
comprises the skin and related organs, the mouth and digestive tract and related organs, the urinary  
and reproductive tracts and related organs, the respiratory tracts and related organs, other internal  
and external tissue surfaces, tissue surfaces exposed during surgery, and tissue with microbial or  
parasitic infection.

Claim 34 (amended). The method of Claim 32 wherein said step of illuminating uses light  
having a wavelength of between approximately 500 nm and 600 nm [green activating light].

Cancel Claim 35.

Claim 36 (amended). A topically-applicable medicament comprising at least one halogenated xanthene as a photoactive [primary active] component, wherein such medicament is useful for photodynamic treatment of human and animal tissue.

Claim 37 (amended). A topically-applicable medicament comprising at least one halogenated xanthene as a primary active component, wherein such medicament is useful for photodynamic treatment of indications selected from the group consisting of diseases of [conditions affecting] the skin and related organs, diseases of [conditions affecting] the mouth and digestive tract and related organs, diseases of [conditions affecting] the urinary and reproductive tracts and related organs, diseases of [conditions affecting] the respiratory tracts and related organs, diseases of [conditions affecting] other internal and external tissue surfaces, [conditions affecting] tissue surfaces exposed during surgery, and [conditions related to] microbial or parasitic infection.